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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/700,971	11/04/2003	Muthiah Manoharan	CHEM0005US.P1	4943
88395	7590	09/29/2009		
Woodcock Washburn LLP Cira Centre, 12th Floor 2929 Arch Street Philadelphia, PA 19104			EXAMINER	
			MCGARRY, SEAN	
			ART UNIT	PAPER NUMBER
			1635	
			MAIL DATE	DELIVERY MODE
			09/29/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

**Advisory Action
Before the Filing of an Appeal Brief**

Application No.

10/700,971

Applicant(s)

MANOHARAN ET AL.

Examiner

Sean R. McGarry

Art Unit

1635

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 10 July 2009 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
(a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
(b) ☐ They raise the issue of new matter (see NOTE below);
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☐ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
The status of the claim(s) is (or will be) as follows:
Claim(s) allowed: _____.
Claim(s) objected to: _____.
Claim(s) rejected: _____.
Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:
See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____.
13. ☐ Other: _____.

/Sean R McGarry/
Primary Examiner, Art Unit 1635

Continuation of 11, does NOT place the application in condition for allowance because: Applicant has provided new arguments in the after final response filed 7/10/09. Applicant argues that the examiner has engaged in hindsight and offers that the art was unpredictable at the time of invention. Applicant offers that neither Tuschl or Beach disclose conjugation of cholesterol to a double stranded oligonucleotide and that Monoharan only discloses conjugation of cholesterol to a single stranded oligonucleotide. Tuschl is relied upon to teach siRNA molecules and the teaching that known methods of nucleic delivery were taught to be useful for delivering siRNA to cells. Tuschl also teaches where an siRNA may be modified such that it does not lose its inhibitory capacity. Beach also teach siRNA like compounds and teach that lipid mediated delivery can be used. Monoharan is relied upon to show that cholesterol conjugation was known in the art to provide enhanced cellular delivery of oligonucleotides which was desirable at the time of invention. Applicant provides a discussion of the difference in modes of action of antisense[RNAse H oligos] and siRNA and assert that one would not utilize modification known for RNAse H oligonucleotides for siRNA compounds. It is noted that the modification at hand has nothing to do with RNAseH activity and is taught by the prior art for increasing cellular uptake. The prior art teaches that cholesterol conjugates are utilized at positions of RNAse H compounds such that they do not interfere with RNAse activity. Tuschl teaches where siRNA compounds can be modified such that siRNA activity is not affected. The rejection is clear that the motivation of cholesterol conjugation is for enhance cellular delivery. Applicant assert that there is no reason one in the art would choose the specified cholesterol from among countless possible modification known in the art. Monoharan teaches that cholesterol conjugation provides enhanced cellular uptake. Applicant argues that the art was unpredictable and one would not expect success in the utilization of the known cholesterol conjugation in an siRNA. This is in opposition to applicants own disclosure. Applicant provides no example of a cholesterol conjugated siRNA and further it suggests hundreds of potential conjugates (known in the art to be used with RNAse H oligonucleotides) and further at paragraph 76 it is asserted that any of these moities can be utilized anywhere in their oligomeric compounds. The rejection is maintained for the reasons of record

/Sean McGarry/
Primary Examiner, Art Unit 1635 .

/Sean McGarry/
Primary Examiner AU1635